REMARKS

Claims 1, 2, and 4-24 are pending. Claims 1, 2 and 4-24 are under examination. Without further addressing the rejections set forth in the Office Action, claims 1 and 11 have been amended without prejudice to Applicants pursuing the previously pending claims in a related application. Claim 14 has been amended to correct a typographical error. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendments to claims 1 and 11 can be found, for example, on page 15, lines 28-31, Table 1 on page 117, in particular SEQ ID NOS:40-42, and claim 11. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1, 2, 4, 5 and 11 under 35 U.S.C. § 102(b) as allegedly anticipated by Hatakeyama et al., Front. Sci. Ser. 29:173-174 (2000), is respectfully traversed. Applicants respectfully submit that the claimed compounds are novel over Hatakeyama et al.

Claim 1, as amended, is directed to a compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising a portion having at least 8 contiguous nucleobases complementary within nucleotides 771-841 of SEQ ID NO: 3 and wherein the compound inhibits the expression of hydroxysteroid 11-beta dehydrogenase 1. Claim 11, as amended, is directed to a compound 12 to 30 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1.

In the Office Action on page 3, the Examiner asserts that the prior art discloses an antisense oligonucleotide that encompasses the start codon of the target nucleic acid and that the oligonucleotide is therefore considered to target/hybridize within the coding region of the target nucleic acid. In order to further prosecution, claims 1 and 11 have been amended to recite that the compounds are complementary to or hybridize within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1. Therefore, Applicants respectfully submit

that this rejection has been rendered moot.[1] Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claim 11 under 35 U.S.C. § 102(a) as allegedly anticipated by Souness et al., Steroids 67:195-201 (2002), is respectfully traversed. Applicants respectfully submit that the claimed compounds are novel over Souness et al.

In the Office Action on page 4, the Examiner asserts that the prior art discloses an antisense oligonucleotide that encompasses the start codon of the target nucleic acid and that the oligonucleotide is therefore considered to target/hybridize within the coding region of the target nucleic acid. The specification teaches that the coding region is between the translation initiation codon and the translation termination codon (page 9, lines 4-8). Nevertheless, to further prosecution, claim 11 has been amended to recite that the compound hybridizes within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1. Accordingly, Applicants respectfully submit that this rejection has been rendered moot and request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claims 1, 2, 4-14 and 21-24 under 35 U.S.C. § 103 as allegedly obvious over Souness et al., *supra*, Hatakeyama et al., *supra*, Bennett et al., U.S. Patent No. 5,998,148, and Baracchini et al., U.S. Patent No. 5,801,154, is respectfully traversed. Applicants respectfully submit that the claimed compounds are unobvious over Souness et al., Hatakeyam et al., Bennett et al. or Baracchini et al., alone or in combination.

First with respect to Souness et al. and Hatakeyama et al. and as discussed above, neither of these references teaches or suggests a compound comprising a modified oliogonucleotide having a nucleobase sequence complementary to or a compound that specifically hybridizes within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1, as recited in amended claim 1 and 11. Furthermore, Applicants respectfully maintain that neither

[1] Applicants' representative wishes to clarify the record that the characterization of Hatakeyama et al. set forth in the previous response as not teaching a compound having a nucleobase sequence complementary to or which specifically hybridizes with a coding sequence of a nucleic acid molecule encoding hydroxysteroid 11-beta dehydrogenase 1 was incorrect. Nevertheless, this has been rendered moot by the amendment to claims 1 and 11.

of Baracchini et al. nor Bennett et al. can cure the deficiencies of Souness et al. or Hatakeyama et al.

On page 8 of the Office Action, it is alleged that the tables in Baracchini et al. and Bennett et al. show that it is not unexpected to obtain antisense compounds that inhibit by at least 51%. Applicants respectfully disagree. First with respect to Baracchini et al., the tables in this reference disclose various antisense oligonucleotides, their sequences, and the target sites in multidrug resistance-associated protein (MRP). However, none of the tables of Baracchini et al. provide any teaching or suggestion of the activity of the oligonucleotides, let alone any teaching or suggestion that it is not unexpected to obtain antisense compounds that inhibit by at least 51%. With regard to Bennett et al., this is the only reference that discloses any specific antisense compounds to a target or the activity of such compounds. In particular, Bennett et al. describes in Table 1, columns 39-40, the inhibitory activity of oligonucleotides targeting microtubule-associated protein 4. Taking the average level of inhibition of regions shown in Table 1 of Bennett et al., the level of inhibition for the 5'UTR was about 45%, for the coding region was about 42%, and for the 3'UTR was about 37%. In contrast to Bennett et al., compounds that are complementary to or that hybridize within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1 as recited in claims 1 and 11, respectively, exhibited an average of about 84% inhibition (Table 1, page 117, SEQ ID NOS:40-42). Based on the description in Souness et al., Hatakeyama et al., Baracchini et al. and/or Bennett et al., one skilled in the art would have had no expectation of the unexpected property of high inhibitory activity of the claimed compounds that have a nucleobase sequence complementary to or that hybridizes within nucleotides 771-841 of SEQ ID NO:3 encoding hydroxysteroid 11-beta dehydrogenase 1. Therefore, Applicants respectfully submit that the claimed compounds are unobvious over Souness et al., Hatakeyama et al., Bennett et al. and/or Baracchini et al., alone or in combination. Accordingly, Applicants respectfully request that this rejection be withdrawn

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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